REMARKS

Claims 1-5, 7, 10, 15, 16, 19, 20, and 23-34 are pending. A copy is attached as Appendix A for your convenience.

The Rejection

Claims 1-5, 7, 10, 15, 16, 19, 20, and 23-34 Are Rejected Under 35 U.S.C. 103(a)

All claims remain rejected over Timpe U.S. Patent No. 6,063,404. The Examiner notes that "Applicant argues that the combination of polymers gives the instant invention the extended release property ... [and] that since Timpe does not teach or suggest the combination of the two polymers ... the prior art invention would not have the extended release property." The Examiner also states that in column 3, lines 3-43, Timpe suggests mixing the two claimed polymers. Therefore, the Examiner concludes, "Timpe's invention would have the extended release property offered by the instant invention."

Applicants respectfully disagree. The invention has two requirements in this regard. The particular combination of polymers provides extended release, and the polymers are combined in a manner that provides progressive hydration. Timpe would not be understood by one of ordinary skill in the art to teach, suggest, or disclose use of the particular combination of polymers, or their combination to provide progressive hydration. In stark contrast, Timpe's focus and goal -- rapid release and bioavailability -- are completely inconsistent with a progressive hydration preparation.

1. This Invention

All pending claims address or use progressive hydration, sustained release pharmaceutical compositions that include both a bioadhesive water insoluble, water swellable cross-linked polycarboxylic polymer, and a water soluble polymer. This particular combination of polymers allows the extended bioadhesion and sustained release

provided by the formulation, and may be -- but does not have to be -- combined in a manner that also provides progressive hydration of the treating agent. The instant invention goes further, and specifically prepares and uses this combination in a manner that results in a formulation that provides both bioadhesive, extended release, and progressive hydration, of the treating agent.

In contrast, there is no prior art of record -- including Timpe -- or otherwise known to the applicants that discloses or teaches use of this particular combination of polymers in an extended release formulation at all, let alone in a manner that provides progressive hydration.

As discussed in prior Responses, most tabletting methods -- including those generally used -- are "wet" methods that, *per se*, do not provide progressive hydration. But wet methods provide convenience, economy, and safety, compared to most "dry" methods. Accordingly, one of ordinary skill in the art would not expect even a disclosure of an extended release formulation containing the same two polymers to teach, disclose, or suggest progressive hydration of the treating agent.

2. Timpe

The Examiner cites Timpe at column 3, lines 3-43, for the proposition that Timpe teaches mixing of the two claimed types of polymers. However, Timpe does not teach use of the particular combination of polymers at all, let alone in a manner that provides progressive hydration.

Timpe simply fails on several levels to teach, disclose, or suggest that: (a) at least two bioadhesive adjuvants should be used; (b) a combination of polymers -- at least one water insoluble and one water soluble -- should be used; (c) the water insoluble polymer should also be a water swellable cross-linked polycarboxylic polymer; or (d) these two polymers should be combined so as to provide progressive hydration of the treating agent.

First, Timpe does not disclose use of the two claimed polymers. At column 3, lines 3-43, Timpe states that the "bioadhesive adjuvant should preferably be a substance that develops adhesion when coming into contact with the mucosa, such as a cellulose, a cellulose derivative, a carboxyvinyl polymer, a derivative of a carboxyvinyl polymer, a lectin or natural material or mixtures of said substances." Lines 3-8; see also, lines 36-43 (emphasis added). Timpe also states that "[a]nother object of the present invention is a method for producing bioadhesive tablets which includes intermixing at least one bioadhesive adjuvant." Lines 31-33 (emphasis added).

Thus, Timpe's disclosure teaches use of at least one bioadhesive adjuvant, selected from a list of broad types of such adjuvants -- most of which would not fall within the instant claims. Nowhere does Timpe further narrow the selection, preference, or quantity of the bioadhesive adjuvants. Thus nowhere does Timpe teach, use, or suggest the particular combination of polymers claimed here, or preparation of the formulation to provide progressive hydration.

Instead, Timpe's broad list of bioadhesive adjuvants -- to be used individually or in combination -- is much broader than the limitations of the instant claims. Three quarters of Timpe's list -- a cellulose or derivative, a lectin, or natural material -- are not polymers at all. The only "polymers" listed are carboxyvinyl polymers and derivatives.

And even focusing on the small portion of Timpe's list that includes polymers, certain of Timpe's polymers may be water soluble, but only other polymers from the very same Timpe category might serve as the water insoluble, water swellable cross-linked polycarboxylic polymer. Thus, for Timpe to be deemed to teach or disclose the instant invention, one of ordinary skill in the art would have to read Timpe's disclosure, of "one or more" bioadhesive adjuvants from a list of four broad categories, to specifically teach or disclose use of at least two polymers from the same Timpe category, including (a) at least

one water soluble polymer, and (b) at least one water insoluble, water swellable cross-linked polycarboxylic polymer. Clearly, this is not a plausible understanding of Timpe's text and teachings.

Second, as discussed thoroughly in prior Responses, Timpe's focus is a quick release formulation for quick bioavailability of the treating agent. This is the very the opposite of a progressive hydration formulation, which is intended to make the treating agent bioavailable slowly, over an extended time. Clearly, Timpe would not use or teach an unusual or burdensome method for formulating the product to provide progessive hydration -- which would be inconsistent with Timpe's desired results. And accordingly, there is absolutely no disclosure, suggestion, or teaching in Timpe of a progressive hydration formulation or result.

Instead, Timpe notes that his invention "can be produced in a known way," or that his pharmaceuticals "are produced in a generally known way ... using the common solid or liquid substrates or diluents and adjuvants commonly used in pharamceutical engineering." Column 4, lines 13-14, and 41-45. Indeed, if there is any significance to Timpe, it is that Timpe's focus on quick bioavailability and on "generally known" methods of formulation essentially teach away from the instant invention for any use contemplated by Timpe.

Thus, while Timpe's broad list of bioadhesive adjuvants may generally cover some of both types of polymers claimed here, Timpe simply does not disclose or teach the particular polymers required by the instant claims, or their combination in a manner designed to provide progressive hydration. Applicants respectfully request reconsideration and withdrawal of this rejection.

Conclusion

In light of these remarks, Applicants respectfully request reconsideration and withdrawal of the rejection, and allowance of all claims.

No fee is believed to be due for this submission. If there are any fees due, please charge the required fees to Winston & Strawn Deposit Account No. 501-814.

Respectfully submitted,

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APPENDIX A

Pending Claims: 1-5, 7, 10, 15-16, 19-20, 23-34

1. (Four times amended) A bioadhesive, controlled, sustained release progressive hydration pharmaceutical composition in the form of a tablet, comprising:

an effective amount of an active ingredient that is a sex hormone,
a bioadhesive, water insoluble, water-swellable cross-linked polycarboxylic polymer, and
a water soluble polymer,

wherein said composition is formulated in a dry state to deliver, upon administration of said tablet to a mucosal surface of a mammal, said active ingredient to the bloodstream of said mammal.

2. The composition of claim 1, wherein said active ingredient is present in about 50% by weight or less.

3. The composition of claim 1, wherein active ingredient is testosterone or progesterone.

4. The composition of claim 3, wherein said composition is formulated to deliver said active ingredient via the mammal's vaginal cavity.

5. The composition of claim 3, wherein said composition is formulated to deliver said active ingredient via the mammal's buccal cavity.

7. (Twice amended) A method of delivering to a mammal a sex hormone, comprising administering said sex hormone via a progressive hydration bioadhesive composition to a mucosal surface of the mammal, wherein said composition is formulated as a dry tablet that includes

(a) said sex hormone,
(b) a bioadhesive, water insoluble, water swellable cross-linked polycarboxylic polymer, and
(c) a water-soluble polymer.

10. (Twice amended) A method of delivering testosterone to a mammal, comprising administering said testosterone via a bioadhesive, progressive hydration composition through a mucosal surface of the mammal, wherein the composition comprises:

a bioadhesive, water insoluble, water-swellable cross-linked polycarboxylic polymer,
a water soluble polymer, and
said testosterone,

and wherein said method provides a blood serum concentration ration of testosterone to 5α-dydrotestosterone (DHT) of about 10 to 1 or greater in the bloodstream of said mammal.

15. (Amended) The composition of claim 1, wherein said composition is formulated to deliver said active ingredient via the mammal's nasal cavity.

16. (Amended) The composition of claim 1, wherein said composition is formulated to deliver said active ingredient via said mammal's rectal cavity.

19. The method of claim 10, wherein said composition is administered through the mammal's buccal cavity.

20. The method of claim 10, wherein said composition is formulated is administered through the mammal's vaginal cavity.

23. (Twice amended) A bioadhesive, progressive hydration pharmaceutical composition comprising:

testosterone,
a bioadhesive, water insoluble, water-swellable cross-linked polycarboxylic polymer,
and a water soluble polymer,

wherein said composition is formulated to progressively hydrate and to deliver a therapeutically effective amount of said testosterone to the bloodstream of a mammal through a mucosal surface of the mammal.

24. The pharmaceutical composition of claim 23, wherein said composition is formulated to deliver said testosterone via the mammal's buccal cavity.

25. The pharmaceutical composition of claim 23, wherein said composition is formulated to deliver said testosterone via the mammal's vaginal cavity.

26. (Amended) A bioadhesive, controlled, sustained release progressive hydration composition for delivering testosterone to the bloodstream of a mammal, comprising:

a bioadhesive, water insoluble, water swellable cross-linked polycarboxylic polymer,
a water soluble polymer,
and testosterone,

wherein said composition is formulated to deliver said testosterone through a mucosal surface of the mammal, and to provide a blood serum concentration ratio of testosterone to 5α-dihydrotestosterone (DHT) of about 10 to 1 or greater in the bloodstream of said mammal.

27. The controlled, sustained release progressive hydration composition of claim 26, wherein said composition is formulated to deliver said testosterone via the mammal's buccal cavity.

28. The controlled, sustained release progressive hydration composition of claim 26, wherein said composition is formulated to deliver said testosterone via the mammal's vaginal cavity.

29. The method of claim 7, wherein said mucosal surface is the mammal's vaginal cavity.

30. The method of claim 7, wherein said mucosal surface is the mammal's buccal cavity.

31. A bioadhesive, progressive hydration pharmaceutical composition comprising:

testosterone,
polycarbophil,
and a water soluble polymer,

wherein said composition is formulated to progressively hydrate and to deliver said testosterone to the bloodstream of a mammal through a mucosal surface of the mammal.

32. The composition of claim 31, wherein the water soluble polymer is carbomer 974P.

33. A method of administering testosterone to a mammal, comprising delivery of said testosterone via a progressive hydration bioadhesive composition to a mucosal surface of said mammal, wherein said composition includes

(a) said testosterone,
(b) polycarbophil, and
(c) a water soluble polymer.

34. The method of claim 33, wherein said water soluble polymer is carbomer 974P.